NATIONAL GUIDELINE CLEARINGHOUSE™ (NGC) GUIDELINE SYNTHESIS

SCREENING FOR COLORECTAL CANCER

GUIDELINES BEING COMPARED

1. **American Cancer Society/US Multisociety Task Force on Colorectal Cancer/American College of Radiology (ACS/USMSTF/ACR)**. Screening and surveillance for the early detection of colorectal cancer and adenomatous polyps, 2008: a joint guideline from the American Cancer Society, the US Multi-Society Task Force on Colorectal Cancer, and the American College of Radiology. CA Cancer J Clin 2008 May-Jun;58(3):130-60. [210 references]
2. **Kaiser Permanente Care Management Institute (KPCMI)**. Colorectal cancer screening clinical practice guideline. Oakland (CA): Kaiser Permanente Care Management Institute; 2008 Dec. 190 p. [195 references]
3. **US Preventive Services Task Force (USPSTF)**. Screening for colorectal cancer: U.S. Preventive Services Task Force recommendation statement. Ann Intern Med 2008 Nov 4;149(9):627-37.

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AREAS OF AGREEMENT AND DIFFERENCE

The American Cancer Society/US Multisociety Task Force on Colorectal Cancer/American College of Radiology (ACS/USMSTF/ACR), Kaiser Permanente Care Management Institute (KPCMI) and the US Preventive Services Task Force (USPSTF) present recommendations for screening in asymptomatic adults at average risk of developing colorectal cancer. While they are beyond the scope of this synthesis, recommendations on screening in groups at increased risk of CRC are provided in the KPCMI guideline. ACS/USMSTF/ACR focused on screening in average risk adults and did not review recent literature on CRC screening or surveillance for individuals at increased and high risk. They advise individuals at increased risk to follow recommendations issued previously by the ACS or USMSTF, which are summarized in Table 3 of the original guideline document.

Areas of Agreement

When to Initiate and Discontinue Screening

All three groups recommend that screening for CRC in average risk, asymptomatic adults should begin at age 50. Recommendations regarding discontinuation are similar, with KPCMI and USPSTF in agreement that routine screening should continue until age 75. For adults with no history of routine screening, however, KPCMI recommends discontinuation at age 80. They note that this decision should be based on physician judgment, patient preference, the increased risk of complications in older adults, and existing comorbidities. USPSTF recommends against routine screening in adults 76 to 85 years, noting that there may be considerations that support CRC screening in an individual patient. ACS/USMSTF/ACR states that if colonoscopy is contraindicated because the patient is not likely to benefit from screening due to life-limiting comorbidity, then neither CTC nor any other CRC screening test is appropriate.

Screening Tests and Frequency

All three groups agree that high-sensitivity gFOBT, FIT, FSIG, colonoscopy, or combined use of these tests, are acceptable options for CRC screening in asymptomatic, average-risk adults.

Recommendations regarding screening intervals are similar. ACS/USMSTF/ACR and KPCMI recommend a 10-year interval for screening with colonoscopy. With regard to FSIG, ACS/USMSTF/ACR recommends a 5-year interval. They note, however, that in high-quality centers (such as the program operated by Kaiser Permanente in California) where procedures are conducted by properly trained and experienced endoscopists who document regular insertion beyond 40 cm with a good bowel preparation, a 10-year interval between negative exams may be reasonable. KPCMI recommends an interval of at least 10 years. They, note, however, that this differs from the HEDIS recommended interval of every five years and that some regions may choose to offer screening at more frequent intervals. High-sensitivity gFOBT and FIT are recommended to be performed annually by ACS/USMSTF/ACR, while KPCMI recommends an interval of every 1 to 2 years.

There is overall agreement that standard guaiac tests are no longer recommended. USPSTF states that although use of an annual FOBT with a lower sensitivity has been demonstrated to reduce CRC mortality in RCTs, modeling suggests that the number of life-years gained will be greater with the strategies using higher sensitivity tests. According to KPCMI, annual standard guaiac FOBT is a less preferred option because of its low sensitivity and low compliance rates. ACS/USMSTF/ACR similarly notes that commonly used guaiac tests, with or without rehydration, that have not been shown in the literature to detect a majority of prevalent CRC at the time of testing are no longer recommended.

While USPSTF's explicit, graded recommendation statements do not address screening intervals, in the narrative part of its guideline it states that modeling evidence suggests that population screening programs between the ages of 50 and 75 years using any of the following 3 regimens will be approximately equally effective in life-years gained, assuming 100% adherence to the same regimen for

that period: 1) annual high-sensitivity FOBT; 2) FSIG every 5 years combined with high-sensitivity FOBT every 3 years; and 3) screening colonoscopy at intervals of 10 years.

All three groups cite screening using FSIG in combination with high-sensitivity gFOBT or FIT as an appropriate screening option.

Areas of Difference

Screening Tests

Recommendations regarding CTC and fecal DNA testing differ, with ACS/USMSTF/ACR citing them as acceptable screening options, and neither KPCMI nor USPSTF recommending their use. According to ACS/USMSTF/ACR, in previous assessments of the performance of CTC and sDNA, the ACS and USMSTF concluded that data were insufficient to recommend screening with these modalities for average-risk individuals. Based on the accumulation of evidence since that time, however, the expert panel now concludes that there are sufficient data to include them as acceptable options for CRC screening. In contrast to ACS/USMSTF/ACR, KPCMI states that virtual colonoscopy every 10 years and fecal DNA testing every 5 years are not recommended as screening strategies for average-risk adults. The USPSTF concluded that the evidence is insufficient to assess the benefits and harms of CTC and fecal DNA testing as screening modalities for colorectal cancer.

Recommendations regarding ACBE/DCBE differ as well. While ACBE/DCBE performed at 5-year intervals is cited as an acceptable screening option by ACS/USMSTF/ACR, KPCMI, in contrast, states that it is not recommended. According to USPSTF, it did not consider barium enema because it has substantially lower sensitivity than modern test strategies, it has not been subjected to screening trials, and its use as a screening test for colorectal cancer is declining.

COMPARISON OF RECOMMENDATIONS	
SCREENING IN AVERAGE-RISK, ASYMPTOMATIC ADULTS **Abbreviations** **Back to TOC**	
ACS/USMSTF/ACR (2008)	**Testing Options for the Early Detection of Colorectal Cancer and Adenomatous Polyps for Asymptomatic Adults Aged 50 Years and Older** Tests that Detect Adenomatous Polyps and Cancer • FSIG every 5 years • Colonoscopy every 10 years • DCBE every 5 years

- CTC every 5 years

Tests that Primarily Detect Cancer

- Annual gFOBT with high test sensitivity for cancer
- Annual FIT with high test sensitivity for cancer
- sDNA test with high sensitivity for cancer, interval uncertain

Screening Tests for the Detection of CRC

gFOBT — Conclusions and Recommendations. Annual screening with high-sensitivity gFOBT (such as Hemoccult SENSA) that have been shown in the published, peer-reviewed literature to detect a majority of prevalent CRC in an asymptomatic population is an acceptable option for colorectal screening in average-risk adults aged 50 years and older. Any positive test should be followed up with colonoscopy. Individuals should be informed that annual testing is necessary to achieve the fullest potential of this test and that they will need follow-up colonoscopy if test results are positive. Screening for CRC with gFOBT in the office following DRE or as part of a pelvic examination is not recommended and should not be done. Commonly used guaiac tests, with or without rehydration, that have not been shown in the literature to detect a majority of prevalent CRC at the time of testing are no longer recommended.

FIT — Conclusions and Recommendations. Annual screening with FIT that have been shown in the published, peer-reviewed literature to detect a majority of prevalent CRC in an asymptomatic population at the time of testing is an acceptable option for colorectal screening in average risk adults aged 50 years and older. Any positive test should be followed up with colonoscopy. Adults should be informed that annual testing is necessary to achieve the fullest potential of this test and that they will need follow-up colonoscopy if test results are positive.

sDNA — Conclusions and Recommendations. In previous assessments of the performance of sDNA, both the ACS and the USMSTF concluded that data were insufficient to recommend screening with sDNA for average-risk individuals. Based on the accumulation of evidence since the last update of these guidelines, the panel concluded that there now are sufficient data to include sDNA as an acceptable option for CRC screening. As noted above, testing stool for molecular

markers is an evolving technology. New iterations of these tests, either technological enhancements of existing tests or completely new test variants, should be carefully evaluated in order to determine that they meet the criteria of detecting a majority of cancers at the time of screening but also have acceptable performance in a screening cohort. While the manufacturer of the one test that is commercially available currently is recommending a 5-year interval for routine screening between examinations with normal results, the panel concluded that there were insufficient data upon which to endorse this interval. Such an interval was judged by the committee to be appropriate only for a test that has very high sensitivity for both cancer and adenomatous polyps—a standard that has not been documented for sDNA to date. At this time, further research is needed to determine the interval between negative sDNA exams. Based on current evidence, the appropriate interval is uncertain.

Tests for the Detection of Adenomas and CRC

FSIG — Conclusion and Recommendations. FSIG can result in the identification of the majority of prevalent CRC at the time of screening, when the examination reaches the splenic flexure or beyond 40 cm as a reasonable target for insertion and when adenomas in the distal colon are used as an indication for the need for colonoscopy. Although the appropriate interval between normal examinations is uncertain, FSIG is recommended to be performed for screening every 5 years in most clinical settings due to concerns about exam quality and completeness. FSIG can be performed alone, or consideration can be given to combining FSIG performed every 5 years with a highly sensitive gFOBT or FIT performed annually. In high-quality centers (such as the program operated by Kaiser Permanente in California) where procedures are conducted by properly trained and experienced endoscopists who document regular insertion beyond 40 cm with a good bowel preparation, a 10-year interval between negative exams may be reasonable. Individuals should be informed about the limitations of FSIG, including the fact that it examines only the distal colon; that there is a risk, albeit small, of perforation; and that they may experience discomfort during and after the examination. Patients should also understand that the examination achieves higher quality when bowel cleansing follows the same protocol as that for colonoscopy. Finally, patients should be informed that positive test findings will need to be followed up with

colonoscopy.

Colonoscopy—Conclusions and Recommendations. The evidence base to support screening colonoscopy, though indirect, is substantial. The appropriate interval between negative colonoscopy screening exams is uncertain because of lack of long-term follow-up data. At present, colonoscopy every 10 years is an acceptable option for CRC screening in average-risk adults beginning at age 50 years. Individuals should be informed about the limitations of colonoscopy, including the fact that it may miss some cancers and significant adenomas and that there is a risk, albeit small, of perforation, hemorrhage (following polypectomy), subsequent hospitalization, and in very rare circumstances, more serious harms. A full bowel cleansing is necessary prior to colonoscopy. Sedation usually is used to minimize discomfort during the examination, and thus a chaperone is required to provide transportation after the examination.

Imaging Examinations of the Colon and Rectum—DCBE and Computed Tomography

DCBE — Conclusions and Recommendations. DCBE every 5 years is an acceptable option for CRC screening in average-risk adults aged 50 years and older. Discussions with patients should include a description of the test characteristics, the importance of adherence to a thorough colon cleansing, test accuracy, the likelihood of a positive test, and the need for subsequent colonoscopy if the test is abnormal. The choice of DCBE for screening can be made on an individual basis, depending on factors such as personal preference, cost, and the local availability of trained radiologists able to offer a high-quality examination.

CTC — Conclusions and Recommendations. In terms of detection of colon cancer and advanced neoplasia, which is the primary goal of screening for CRC and adenomatous polyps, recent data suggest CTC is comparable to optical colonoscopy for the detection of cancer and polyps of significant size when state-of-the-art techniques are applied. In previous assessments of the performance of CTC, the ACS concluded that data were insufficient to recommend screening with CTC for average-risk individuals. Based on the accumulation of evidence since that time, the expert panel concludes that there are sufficient data to include CTC as an acceptable option for CRC screening.

	Screening of average-risk adults with CTC should commence at age 50 years. The interval for repeat exams after a negative CTC has not been studied and is uncertain. However, if current studies confirm the previously reported high sensitivity for detection of cancer and of polyps 6 mm, it would be reasonable to repeat exams every 5 years if the initial CTC is negative for significant polyps until further studies are completed and are able to provide additional guidance. Until there is more research on the safety of observation, colonoscopy should be offered to patients whose largest polyp is 6 mm or greater. CTC surveillance could be offered to those patients who would benefit from screening but either decline colonoscopy or who are not good candidates for colonoscopy for one or more reasons. However, if colonoscopy is contraindicated because the patient is not likely to benefit from screening due to life-limiting comorbidity, then neither CTC nor any other CRC screening test would be appropriate.
KPCMI (2008)	**Recommendation: Effectiveness of Colorectal Cancer Screening Tests** A. CRC screening is strongly recommended for all asymptomatic, average-risk adults. (**Evidence-based: A**) B. Any of the following tests are acceptable for CRC screening in asymptomatic, average-risk adults:* • High-sensitivity fecal occult blood test. (**Consensus-based**) • Immunochemical fecal occult blood test (iFOBT/FIT).** (**Consensus-based**) • FSIG. (**Evidence-based: B**) • Colonoscopy.** (**Consensus-based**) • A combination of high-sensitivity gFOBT test and FSIG. (**Consensus-based**) C. The following additional screening tests are either less-preferred options or not recommended for screening. However, an adult who has had one of these tests is considered screened. Follow-up screening using a preferred option is recommended. • An annual standard gFOBT is a less-preferred option.*** (**Consensus-based**) • ACBE is not recommended as a screening strategy for average-risk adults. (**Evidence-based: I**) • Virtual colonoscopy is not recommended as a screening strategy for average-risk adults.* (**Consensus-based**) • Fecal DNA is not recommended as a

screening strategy for average-risk adults.****(**Consensus-based**)

Note: For fecal blood tests, inform patients of the potential risks associated with false-positive test and false-negative test results, as well as the need for prompt follow-up of a positive test result. For FSIG, inform patients that the test has a small risk of complications and is not a complete examination of the entire colon.

*There is insufficient evidence to choose one screening test over another.

**If a patient has had a normal colonoscopy within the last 10 years, there is insufficient evidence that supplemental FOBT adds any incremental benefit.

***Even though there is sufficient evidence in support of this screening modality, it is not a preferred option due to its low sensitivity and low compliance rates.

****Please note that fecal DNA testing and virtual colonoscopy are not listed as "appropriate screening tests" in 2008 HEDIS (Health Plan Employer Data and Information Set) specifications for colorectal cancer screening, and therefore regions may choose to screen members with other appropriate tests.

Recommendation: Frequency of Colorectal Cancer Screening

A. The following intervals for colorectal cancer screening in asymptomatic, average-risk adults are recommended*:
    - FSIG: at least every 10 years. (**Consensus-based**)
    - High-sensitivity guaiac or immunochemical FOBT (iFOBT/FIT): every 1-2 years. (**Consensus-based**)
    - Colonoscopy: every 10 years. (**Consensus-based**)
    - Combined FOBT and FSIG: every 1-2 years for FOBT, at least every 10 years for flexible sigmoidoscopy. (**Consensus-based)**
B. The following additional screening tests are either less-preferred options or not recommended for screening. However, if these tests are performed, then the recommended intervals are as indicated below. Follow-up screening using a preferred option is recommended.
    - Standard gFOBT: every 1-2 years. (**Consensus-based**)
    - ACBE:** every 5 years. (**Consensus-**

	based) • Virtual colonoscopy:** every 10 years. (**Consensus-based**) • Fecal DNA:** every 5 years. (**Consensus-based**) * The GDT recognizes that these screening intervals differ from current HEDIS measures. Some regions may choose to offer screening at more frequent intervals. HEDIS intervals are as follows: FOBT (annual), flexible sigmoidoscopy (every 5 years), air contrast barium enema (every 5 years), colonoscopy (every 10 years). **These modalities are not recommended for screening average-risk adults (see Recommendation #2 above). **Recommendation: Age to Begin and End Colorectal Cancer Screening** In the absence of sufficient evidence, the following ages at which to begin and end colorectal cancer screening in asymptomatic average-risk adults are recommended: A. Initiation of screening is recommended at age 50. (**Consensus-based**) B. Discontinuation of screening is generally recommended at age 75, provided that there is a history of routine screening. For those with no history of routine screening, discontinuation is recommended at age 80. The decision to discontinue screening should be based on physician judgment, patient preference, the increased risk of complications in older adults, and existing comorbidities. (**Consensus-based**)
USPSTF (2008)	**Summary of Recommendations** • The USPSTF recommends screening for CRC using FOBT, sigmoidoscopy, or colonoscopy, in adults, beginning at age 50 years and continuing until age 75 years. **Grade: A recommendation.** • The USPSTF recommends against routine screening for CRC cancer in adults age 76 to 85 years. There may be considerations that support colorectal cancer screening in an individual patient. **Grade: C recommendation.** • The USPSTF recommends against screening for CRC in adults older than age 85 years. **Grade: D recommendation.** • The USPSTF concludes that the evidence is insufficient to assess the benefits and harms of CTC

and fecal DNA testing as screening modalities for colorectal cancer. **Grade: I statement.**

Patient Population under Consideration

These recommendations apply to adults 50 years of age and older, excluding those with specific inherited syndromes (the Lynch syndrome or familial adenomatous polyposis) and those with inflammatory bowel disease. The recommendations do apply to those with first-degree relatives who have had colorectal adenomas or cancer, although for those with first-degree relatives who developed cancer at a younger age or those with multiple affected first-degree relatives, an earlier start to screening may be reasonable. Data suggest that colorectal cancer has a higher mortality rate in African Americans. The reasons for this differential are not well known, and the recommendations are intended to apply to all ethnic and racial groups.

When the screening test results in the diagnosis of clinically significant colorectal adenomas or cancer, the patient will be followed by a surveillance regimen and recommendations for screening are no longer applicable. The USPSTF did not address evidence for the effectiveness of any particular surveillance regimen after diagnosis and/or removal of adenomatous polyps.

Screening Tests

The relative sensitivity and specificity of the different colorectal screening tests with adequate data to assess cancer detection — colonoscopy, FSIG, and fecal tests — can be depicted as follows:

Sensitivity: Hemoccult II < FIT ≤ Hemoccult SENSA ~ FSIG < colonoscopy

Specificity: Hemoccult SENSA < FIT ~ Hemoccult II < FSIG = colonoscopy

For the operator-dependent tests—FSIG, CT colonography, and colonoscopy—better operator training and more experience have a high likelihood of improving sensitivity. Approaches related to certification, such as quality standards and possibly minimum volume requirements, could be used to achieve the goal of improving operator performance and therefore test sensitivity. Assurance of performance of

high-quality endoscopy should be part of all screening programs.

Because several screening strategies have similar efficacy, efforts to reduce colon cancer deaths should focus on implementation of strategies that maximize the number of individuals who get screening of some type. The different options for CRC screening tests are variably acceptable to patients; eliciting patient preferences is one step in improving adherence. Ideally, shared decision making between clinicians and patients would incorporate information on local test availability and quality as well as patient preference.

Screening Intervals and Starting and Stopping Ages

Screening programs incorporating FOBT, FSIG, or colonoscopy will all be effective in reducing mortality. Modeling evidence suggests that population screening programs between the ages of 50 and 75 years using any of the following 3 regimens will be approximately equally effective in life-years gained, assuming 100% adherence to the same regimen for that period: 1) annual high-sensitivity FOBT, 2) sigmoidoscopy every 5 years combined with high-sensitivity FOBT every 3 years, and 3) screening colonoscopy at intervals of 10 years.

The strategies differ in the total number of colonoscopies that would be required to gain similar numbers of life-years. The first strategy, use of annual high-sensitivity FOBT (sensitivity for cancer $\geq$ 70%) that has a false-positive rate less than 10% (that is, specificity > 90%), is estimated to require the fewest colonoscopies while achieving a gain in life-years similar to that seen with screening colonoscopy every 10 years. Currently available tests that meet both specifications include SENSA guaiac testing (Beckman Coulter, Fullerton, California) and FIT with characteristics similar to those of the Magstream quantitative test (Fujirebio, Tokyo, Japan).

Although use of an annual FOBT with a lower sensitivity has been demonstrated to reduce CRC mortality in randomized, controlled trials, modeling suggests that the number of life-years gained will be greater with the strategies using higher sensitivity tests.

For all screening modalities, the effectiveness decreases substantially as adherence to the regimen declines. At

	the individual level, adherence to a screening regimen will be more important in life-years gained than will the particular regimen selected. Current data are insufficient to predict adherence to any specific screening regimen at the population level. **Considerations for Practice When Evidence Is Insufficient** *CT Colonography* Potential Preventable Burden. A screening program that incorporates the option of CT colonography could help reduce CRC mortality in the population if patients who would otherwise refuse screening found it an acceptable alternative. Potential Harms. The potential harms from evaluation of incidental findings found with CT colonography may be large. The lifetime cumulative radiation risk from use of CT colonography to screen for CRC should be considered, as well as the growing cumulative radiation exposure from the use of other kinds of diagnostic and screening that involve radiation exposure. Current Practice. CTC performed by trained and experienced radiographers may not be currently available in many parts of the United States. Costs. Patient time and burden to participate in CRC screening using test strategies that require bowel preparation are substantial. A CT colonography screening strategy that did not involve bowel preparation would decrease the burden of adherence. The cost of CT colonography is high. *Fecal DNA* Potential Preventable Burden. Fecal DNA has potential as a highly specific test, and it could reduce harms associated with follow-up of false-positive test results. Current Practice. Fecal DNA tests are evolving, and no test is widely used. Costs. Fecal DNA is likely to have a high monetary cost per test.

<table>
<tr><th colspan="2">STRENGTH OF EVIDENCE AND RECOMMENDATION GRADING SCHEMES
Abbreviations
Back to TOC</th></tr>
<tr><td>ACS/USMSTF/ACR (2008)</td><td>Not applicable</td></tr>
<tr><td>KPCMI (2008)</td><td>Recommendations are classified as either "evidence-based (A-D, I)" or "consensus-based."

• Evidence-based: Sufficient number of high-quality studies from which to draw a conclusion, and the recommended practice is consistent with the findings of the evidence. A recommendation can also be considered "evidence-based" if there is insufficient evidence and no practice is recommended.
• Consensus-based: Insufficient evidence and a practice is recommended based on the consensus or expert opinion of the Guideline Development Team.

Label and Language of Recommendations

<table>
<tr><th>Label</th><th>Evidence-Based Recommendations*</th></tr>
<tr><td>Evidence-based (A)</td><td>Language: [a] The intervention is strongly recommended for eligible patients.

Evidence: The intervention improves important health outcomes, based on good evidence, and the Guideline Development Team (GDT) concludes that benefits substantially outweigh harms and costs.

Evidence Grade: Good.</td></tr>
<tr><td>Evidence-based (B)</td><td>Language: [a] The intervention is recommended for eligible patients.

Evidence: The intervention improves important health outcomes, based on 1) good evidence that benefits outweigh harms and costs; or 2) fair evidence that benefits substantially outweigh harms and costs.

Evidence Grade: Good or Fair.</td></tr>
<tr><td>Evidence-based (C)</td><td>Language: [a] No recommendation for or against routine provision of the intervention. (At the discretion of the GDT, the recommendation may use the language "option," but must list all the equivalent</td></tr>
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		options.) **Evidence**: Evidence is sufficient to determine the benefits, harms, and costs of an intervention, and there is at least fair evidence that the intervention improves important health outcomes. But the GDT concludes that the balance of the benefits, harms, and costs is too close to justify a general recommendation. **Evidence Grade**: Good or Fair.
	Evidence-based (D)	**Language**: [a] Recommendation against routinely providing the intervention to eligible patients. **Evidence**: The GDT found at least fair evidence that the intervention is ineffective, or that harms or costs outweigh benefits. **Evidence Grade**: Good or Fair.
	Evidence-based (I)	**Language**: [a] The evidence is insufficient to recommend for or against routinely providing the intervention. (At the discretion of the GDT, the recommendation may use the language "option," but must list all the equivalent options.) **Evidence**: Evidence that the intervention is effective is lacking, of poor quality, or conflicting and the balance of benefits, harms, and costs cannot be determined. **Evidence Grade**: Insufficient.
	Consensus-based	**Language**: [a] The language of the recommendation is at the discretion of the GDT, subject to approval by the National Guideline Directors. **Evidence**: The level of evidence is assumed to be "Insufficient" unless otherwise stated. However, do not use the A, B, C, D, or I labels which are only intended to be used for evidence-based recommendations. **Evidence Grade**: Insufficient, unless otherwise stated.
	For the rare consensus-based recommendations which have "Good" or "Fair" evidence, the evidence must support a	

different recommendation, because if the evidence were good or fair, the recommendation would usually be evidence-based. In this kind of consensus-based recommendation, the evidence grade should point this out (e.g., "Evidence Grade: Good, supporting a different recommendation").

[a] All statements specify the population for which the recommendation is intended.

*Recommendations should be labeled and given an evidence grade. The evidence grade should appear in the rationale. Evidence is graded with respect to the degree it supports the specific clinical recommendation. For example, there may be good evidence that Drugs 1 and 2 are effective for Condition A, but no evidence that Drug 1 is more effective than Drug 2. If the recommendation is to use either Drug 1 or 2, the evidence is good. If the recommendation is to use Drug 1 in preference to Drug 2, the evidence is insufficient.

USPSTF (2008)

What the United States Preventive Services Task Force (USPSTF) Grades Mean and Suggestions for Practice

Grade	Grade Definitions	Suggestions for Practice
A	The USPSTF recommends the service. There is high certainty that the net benefit is substantial.	Offer or provide this service.
B	The USPSTF recommends the service. There is high certainty that the net benefit is moderate or there is moderate certainty that the net benefit is moderate to substantial.	Offer or provide this service.
C	The USPSTF recommends against routinely providing the service. There may be considerations that support providing the service in an individual patient. There is moderate or high certainty that the net benefit is small.	Offer or provide this service only if other considerations Support offering/providing the service in an individual patient.
D	The USPSTF recommends against	Discourage the use of this service.

	the service. There is moderate or high certainty that the service has no net benefit or that the harms outweigh the benefits.	
I Statement	The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of the service. Evidence is lacking, of poor quality, or conflicting, and the balance of benefits and harms cannot be determined.	Read "Clinical Considerations" section of USPSTF Recommendation Statement (see "Major Recommendations" field). If the service is offered, patients should understand the uncertainty about the balance of benefits and harms.

USPSTF Levels of Certainty Regarding Net Benefit

Definition: The U.S. Preventive Services Task Force defines certainty as "likelihood that the USPSTF assessment of the net benefit of a preventive service is correct." The net benefit is defined as benefit minus harm of the preventive service as implemented in a general, primary care population. The USPSTF assigns a certainty level based on the nature of the overall evidence available to assess the net benefit of a preventive service.

Level of Certainty	Description
High	The available evidence usually includes consistent results from well-designed, well-conducted studies in representative primary care populations. These studies assess the effects of the preventive service on health outcomes. This conclusion is therefore unlikely to be strongly affected by the results of future studies.
Moderate	The available evidence is sufficient to determine the effects of the preventive service on health outcomes, but confidence in the estimate is constrained by factors such as: • The number, size, or quality of individual studies • Inconsistency of findings across individual studies • Limited generalizability of findings to

		routine primary care practice • Lack of coherence in the chain of evidence As more information becomes available, the magnitude or direction of the observed effect could change, and this change may be large enough to alter the conclusion.
	Low	The available evidence is insufficient to assess effects on health outcomes. Evidence is insufficient because of: • The limited number or size of studies • Important flaws in study design or methods • Inconsistency of findings across individual studies • Gaps in the chain of evidence • Findings not generalizable to routine primary care practice • A lack of information on important health outcomes More information may allow an estimation of effects on health outcomes.

COMPARISON OF METHODOLOGY ***Click on the links below for details of guideline development methodology***		
ACS/USMSTF/ACR (2008)	**KPCMI (2008)**	**USPSTF (2008)**
Methods used to collect and select the evidence were similar in that all three groups performed searches of electronic databases and hand searches of published literature (primary sources). USPSTF and KPCMI also performed hand searches of published literature (secondary sources); ACS/USMSTF/ACR performed searches of unpublished data. A targeted, updated systematic evidence review was prepared by the Oregon Evidence-based Practice Center (EPC) for use by the USPSTF in the development of its guideline. To assess the quality and strength of the evidence, ACS/USMSTF/ACR and USPSTF employed expert consensus, while KPCMI weighted the evidence according to a rating scheme. Methods used to analyze the evidence vary, with the exception that USPSTF and KPCMI both performed a systematic review with evidence tables. USPSTF also performed a meta-analysis and utilized decision analysis; KPCMI reviewed published meta-analyses. Both groups provide a description of processes used. ACS/USMSTF/ACR reviewed the literature as a		

means of analysis, but not does provide details of the process. With regard to formulation of guideline recommendations, all three groups utilized expert consensus and provide a description of the formulation process. USPSTF also employed balance sheets. The KPCMI and USPSTF guidelines, in contrast to ACS/USMSTF/ACR, graded the strength of their recommendations according to a rating scheme. None of the groups performed a cost formal cost analysis. ACS/USMSTF/ACR, however, was the only group to review published cost analyses during the development of its guideline. The two groups to specify method(s) of guideline validation, KPCMI and USPSTF, both used internal peer review. USPSTF also used external peer review and comparison with guidelines from other groups.

SOURCE(S) OF FUNDING Abbreviations Back to TOC	
ACS/USMSTF/ACR (2008)	American Cancer Society, U.S. Multi-Society Task Force on Colorectal Cancer, American College of Radiology
KPCMI (2008)	Kaiser Permanente Care Management Institute
USPSTF (2008)	United States Government

BENEFITS AND HARMS Abbreviations Back to TOC	
Benefits	
ACS/USMSTF/ACR (2008)	Screening of average-risk individuals can reduce CRC incidence and mortality by detecting cancer at an early, curable stage and by detecting and removing clinically significant adenomas.
KPCMI (2008)	• Appropriate CRC screening • Early detection of CRC in the general population; asymptomatic, average-risk adults; and increased-risk adults • Reduced morbidity and mortality from CRC

USPSTF (2005)	**Benefits of Detection and Early Intervention** • There is convincing evidence that screening with any of the 3 recommended tests reduces colorectal cancer mortality in adults age 50 to 75 years. Follow-up of positive screening test results requires colonoscopy regardless of the screening test used. Because of the harms of colonoscopy described below, the chief benefit of less invasive screening tests is that they may reduce the number of colonoscopies required and their attendant risks. • There is adequate evidence that the benefits of detection and early intervention decline after age 75. There is a substantial lead time between the detection and treatment of colorectal neoplasia and a mortality benefit, and competing causes of mortality make it progressively less likely that this benefit will be realized with advancing age.
Harms	
ACS/USMSTF/ACR (2008)	**Colonoscopy** • Colonoscopy can result in significant harms, most often associated with polypectomy, and the most common serious complication is postpolypectomy bleeding. • Another significant risk associated with colonoscopy is perforation. • Cardiopulmonary complications represent about one-half of all adverse events that occur during colonoscopy and usually are related to sedation. **gFOBT and FIT** When either the test, the testing procedure, or both have very low test sensitivity and when positive tests are not followed up with colonoscopy, the potential is high for patients to have a false sense of reassurance after testing. **DCBE** Perforation rate is lower than that of colonoscopy (1 of 25,000 versus 1 of 1,000 to 2,000). Caution is advised when performing a DCBE on the same day after polypectomy to avoid a perforation. **CTC**

	• There may be long-term potential harm from radiation dose effects from computed tomography examinations. • Because CTC produces an image not only of the colon but also the upper and lower abdomen, there is a chance that incidental extracolonic findings will be observed. While there are potential benefits from serendipitous findings, there are also associated risks and costs that need to be considered when these findings are false positives. These include further radiologic imaging and, thus, added organ dose, potential for adverse outcomes associated with tissue sampling for abnormalities that are not resolved with additional imaging, as well as the direct and indirect costs to the patient. **FSIG** Complications of flexible sigmoidoscopy include perforation (though risk is small) and periprocedural discomfort.
KPCMI (2008)	• Inconvenience, anxiety, and adverse effects of tests (e.g., discomfort, pain, bowel perforation, bleeding) • Unnecessary invasive tests due to false-positive test results • False reassurance from false-negative test results
USPSTF (2008)	**Harms of Detection and Early Intervention** The primary established harms of colorectal cancer screening are due to the use of invasive procedures initially or in the evaluation sequence. Harms may arise from the preparation the patient undergoes to have the procedure, the sedation used during the procedure, and the procedure itself. *Colonoscopy* Evidence is adequate to estimate the harms of colonoscopy. In the United States, perforation of the colon occurs in an estimated 3.8 per 10,000 procedures. Serious complications—defined as deaths attributable to colonoscopy or adverse events requiring hospital admission, including perforation, major bleeding, diverticulitis, severe abdominal pain, and cardiovascular events—are significantly more common, occurring in an estimated 25 per 10,000 procedures.

	Flexible Sigmoidoscopy Evidence is adequate that serious complications occur in approximately 3.4 per 10,000 procedures. *Fecal Tests* Evidence about the harms of fecal tests is lacking (inadequate), but the U.S. Preventive Services Task Force (USPSTF) assesses them to be no greater than small. *CT Colonography* • Computed tomographic colonography images more than the colon. Up to 16% of people having their first CT colonography are found to have extracolonic abnormalities that require further testing. Evidence is inadequate to assess the clinical consequences of identifying these abnormalities, but there is potential for both benefit and harm. Potential harms arise from additional diagnostic testing and procedures for lesions found incidentally, which may have no clinical significance. This additional testing also has the potential to burden the patient and adversely impact the health system. • The risks for perforation associated with CT colonography in research settings are estimated to be 0 to 6 per 10,000 CT colonography studies. However, these estimates may be higher than what can be expected in screened populations because the studies included symptomatic populations. • Radiation exposure resulting from CT colonography is reported to be 10 mSv per examination. The harms of radiation at this dose are not certain, but the linear-no-threshold model predicts that 1 additional individual per 1000 would develop cancer in his or her lifetime at this level of exposure. The lifetime cumulative radiation risk from the use of CT colonography to screen for colorectal cancer should be considered in the context of the growing cumulative radiation exposure from the use of other diagnostic and screening tests that involve radiation exposure. On the other hand, improvements in CT colonography technology and practice are lowering this radiation dose.

Abbreviations
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ACBE, Air contrast barium enema

ACS, American Cancer Society

ACR, American College of Radiology

CRC, colorectal cancer

CTC, computed tomographic colonography (virtual colonoscopy)

DCBE, double contrast barium enema

DRE, digital rectal examination

FAP, familial adenomatous polyposis

FIT, fecal immunochemical test

FSIG, flexible sigmoidoscopy

GDT, Guideline Development Team

gFOBT, guaiac-based FOBT

FOBT, fecal occult blood testing

IBD, inflammatory bowel disease

KPCMI, Kaiser Permanente Care Management Institute

HNPCC, hereditary nonpolyposis colorectal cancer

sDNA, stool DNA

USMSTF, U.S. Multi-Society Task Force on Colorectal Cancer

USPSTF, U.S. Preventive Services Task Force

This synthesis was prepared by ECRI Institute on November 15, 2007. It was reviewed by UMHS on December 4, 2007, and by ICSI on December 14, 2007. This synthesis was updated in August 2009 to remove ICSI recommendations and to add ACOG recommendations. This synthesis was revised in September 2009 to add ACS/USMSTF/ACR, KPCMI and USPSTF recommendations. The information was verified by USPSTF on October 28, 2009 and by ACS/USMSTF/ACR on November 11, 2009.

Internet citation: National Guideline Clearinghouse (NGC). Guideline synthesis: Screening for colorectal cancer. In: National Guideline Clearinghouse (NGC)

[website]. Rockville (MD): 1998 Jun (revised 2009 Dec) [cited YYYY Mon DD]. Available: http://www.guideline.gov.

Date Modified: 12/7/2009